UNITED STATES DISTRICT COURT
EASTERN DISTRICT OF MISSOURI

IN RE: LEXAPRO AND CELEXA PRODUCTS LIABILITY LITIGATION	§	**MDL No. 4:06-md-01736-RWS**
THIS DOCUMENT APPLIES TO: ALL ACTIONS	§	

PLAINTIFFS' MEMORANDUM IN OPPOSITION TO DEFENDANTS' MOTION TO EXCLUDE TESTIMONY OF PLAINTIFF'S EXPERT, DAVID HEALY, M.D.

Plaintiffs respond to Defendants Forest Laboratories, Inc., and Forest Pharmaceuticals, Inc., [collectively hereinafter "Forest"] Motion to Exclude Plaintiffs' general causation expert, Dr. David Healy, as follows:

Overview and Summary

Forest has filed a *"Daubert"* Motion to Exclude the "general causation" opinion testimony of the internationally renowned and widely published neuro-psychopharmacologist, Dr. David Healy. [Doc.#623.][1] The key opinion that Forest seeks to exclude is that the twin SSRI drugs Celexa[2] and Lexapro[3] "can cause some people to commit suicide." This is, of course, a critical ultimate issue of fact for the jury in each of the remaining cases in this long pending MDL.

Indeed, it was this very question that the jury in *Tobin v. SmithKlineBeecham* answered in the affirmative in their June 4, 2001 verdict. Exhibit 1 at 1 (*Tobin* Verdict dated 06.06.01). The key expert testimony that supported that verdict was that of Dr. David Healy. Magistrate Judge Beaman

---

[1] Forest has concurrently sought to exclude the testimony of Plaintiffs' warnings expert, Dr. Michael Hamrell. [Doc. #626]. All arguments, authorities, and exhibits in Plaintiffs concurrently filed Opposition to that motion are expressly incorporated herein.

[2] The generic name for Celexa is citalopram.

[3] The generic name for Lexapro is escitalopram.

rejected SKB's *Daubert* challenges to that testimony. Exhibit 2 (*Tobin Daubert* Order dated 05.01.01). He was in good company. Up until that time, every other federal judge that had considered challenges to similar testimony from Dr. Healy had equally rejected them.[4] Indeed, one of them, Chief Judge Donette Ambrose in the Western District of Pennsylvania, even found that Dr. Healy's opinions concerning SSRIs and suicidality were "generally accepted" within the meaning of *Daubert* and its more stringent precursor *Frye*. Exhibit 4 at 1 (*Cassidy Daubert* Order dated 06.04.02).

To combat this weight of judicial precedents, Forest cites the late 2001 decision of Judge Kathryn Vratil in the Zoloft case of *Miller v. Pfizer, Inc.*, 356 F.3d 1326 (10th Cir. 2004). As explained in more detail *infra*, the discretionary decision to exclude Dr. Healy's testimony in this tragic case can, with the benefit of hind-sight, only be described as a very sad miscarriage of justice. *Miller* involved the death of a 13 year old boy. The plaintiffs in that case argued for court appointment of independent experts, at the inception of the case, to scrutinize the testimony of *both sides'* experts. Exhibit 5 at 1 (Vickery Affidavit). But the trial judge waited until much later in the case, and then only tasked the experts with advising her with respect to Dr. Healy's testimony. *Id*. Then, in the evidentiary hearing, when one of the court's experts asked a question which Dr. Healy was perfectly happy to answer and explain, the judge refused to permit him to answer that question, based on her strained interpretation of Rule 26, *i.e.,* that an expert must *anticipate* all questions that might be asked about his/her methodology and address them all in the report. Exhibit 6 at 389-92 (*Miller* Transcript dated 11.20.01).

---

[4] Dr. Healy's first testimony in a SSRI suicide case was in the 1999 trial of *Forsyth v. Lilly*. The case was tried in Hawaii and the *Daubert* challenges were launched in the era of *Daubert II*. Chief Judge Kay rejected Lilly's attempts to disqualify Dr Healy. Exhibit 3 at 24-25 (Forsyth *Daubert* Order date 01.05.98). One of the reasons that he did so was that epidemiological data from Professor Jick showed a relative risk for Prozac (fluoxetine)-induced suicidality of 2.1+. *Id.* at 21.

The sequella to the *Miller* decision confirm the injustice. First, the FDA, based in part on the same reasoning and opinions from Dr. Healy, and after considering Pfizer's "anti-Healy" diatribe brief, found in 2004 that the SSRI's can and do cause some younger patients, like 13 year old Matthew Miller, to commit suicide "DUE TO DRUG." Exhibit 7 (Healy Letter to FDA); Exhibit 8 at 5-6 (Sept 2004 FDA Minutes); Exhibit 9 (July 2005 Celexa HCP Alert); Exhibit 10 (July 2005 Lexapro HCP Alert). As a result it required class-wide **BLACK BOX WARNINGS** about this very risk. Exhibit 11 at 1-2 (FDA Oct 2004 letter). Second, one of the court-appointed experts in *Miller*, Dr. John Davis, was so concerned about the potential misuse of this precedent that he wrote a pro bono "friend of the court" letter to a federal judge who was considering a similar motion to exclude Dr. Healy.[5] Exhibit 12 (Davis Letter dated 01.16.07).

But to really frame the incongruity and disingenuous nature of Forest's motion, the Court need only examine the following testimony from Dr. Chris Muldoon, the Interim Medical Affairs Manager and former Medical Director for Lundbeck.[6] Dr. Muldoon was appearing on behalf of Lundbeck at an official inquest in the United Kingdom. Therein, Dr. Muldoon, who gained personal experience with Celexa clinical research while employed by Lundbeck per his own testimony, was asked the following question:

Q "Do you believe that citalopram can cause somebody who would not otherwise take their own life to do so?"

A "Yes."

---

[5] The other "independent" expert, Dr. John Concato, has been retained by Forest in this litigation. For a fee of $300/hour he has written a 28 page report that (a) sets forth no substantive opinions of his own regarding the causality issues in this case, but (b) critiques Dr. Healy's opinions at length. *See generally* Exhibit 35. Fortunately, his trial testimony will be subject to cross examination.

[6] Lundbeck is the Danish company that developed Celexa and through whom Forest was licensed to market the product in the United States. Exhibit 13 at 12 (Healy Expert Report).

Id. at 46-47, 52. Dr. Healy not only was present for this testimony, but he specifically incorporated it in his expert report. *Id*. The notion that Dr. Healy's testimony is unreliable is utterly belied by the testimony of a senior executive from Forest's business and strategic partner. For the reasons, and on the authorities, set forth more fully below, Forest's motion in this case should be DENIED in all respects.

Introduction

In *Daubert v. Merrell Dow*,[7] Merrell Dow argued for a return to *Frye* and the scientific orthodoxy of "general acceptance." The Supreme Court rejected that notion with a more common sense approach that focused on four factors that will be discussed more fully below. *Id.* at 592-94. In *Kumho,*[8] the Court added a fifth factor that some courts and commentators have suggested is the closest thing to a litmus test that there is, *i.e.,* whether the expert utilizes the same level of "intellectual rigor" in testifying that he/she does in his normal professional activities.

There were some who believed that *Daubert* wrought a significant change in the law. However, seventeen years after the decision was handed down, the Official Comments to the 2000 amendments to Rule 702, FED. R. EVID., expressed a very different view. Rejecting the notion of some, that the four *Daubert* factors be enshrined into the rule as essential factors for the admissibility of all expert testimony, the Supreme Court reiterated that "all of these factors remain relevant . . . yet no single factor is necessarily dispositive." *Daubert,* 509 U.S. at 594. Moreover, in spite of the fact that *Daubert* motions have become *de rigeur* tactics for pharmaceutical companies, the Supreme Court's comments reflected that "a review of the case law after *Daubert* shows that the rejection of expert testimony is the exception rather than the rule. *Daubert* did not work a 'seachange over

[7] 509 U.S. 579 (1993).

[8] *Kumho Tire Co. v. Carmichael*, 526 U.S. 137, 152 (1999).

federal evidence law,' and 'the trial court's role as gatekeeper is not intended to serve as a replacement for the adversary system." Official Comments to 2000 Amendment to Rule 702, FED. R. EVID. *Accord McIntosh v Monsanto Co.,* 462 F Supp 2d 1025, 1032 (E.D. Mo. 2006)("a review of the case law after *Daubert* shows that the rejection of expert testimony is the exception rather than the rule.").

This is, of course, fully consistent with the views of how to harmonize "Law" and "Science" as set forth in the 2011 Federal REFERENCE MANUAL ON SCIENTIFIC EVIDENCE: THIRD EDITION. As Justice Breyer himself recognized in his Introduction, if a court adopts arguments that are too narrow and precise for the very scientific orthodoxy that was rejected by the Supreme Court in *Daubert*, and if that results in a discretionary, exclusionary, dispositive ruling, it may wreak havoc with the entire system:

> A decision wrongfully denying compensation in a toxic substance case, for example, cannot only deprive the plaintiff of warranted compensation but also discourage other similarly situated individuals from even trying to obtain compensation and encourage the continued use of a dangerous substance.

Id. at 4. To help courts and counsel strike the right balance, Justice Breyer elaborated that "the search is not a search for scientific precision. . . .The law must seek decisions that fall within the boundaries of scientifically sound knowledge.... Furthermore, science itself may be highly uncertain and controversial with respect to many of the matters that come before the courts." *Id*. And, more importantly, he reminds us all that the exercise of judicial discretion in the *Daubert* context must be made with a keen Article III sensitivity to the "basic human liberties . . . guaranteed by our Constitution's Seventh Amended . . . the right to a trial by jury." *Id*. at 5. He adds,

> Any effort to bring better science into the courtroom must respect the jury's constitutionally specified role – even if doing so means that, from a scientific perspective, an incorrect result is sometimes produced.

Id.[9]

There are, of course, a myriad of federal opinions that cite *Daubert* and its progeny. A comprehensive review of the case law would be never ending. However, there are two recent opinions that, at the outset, merit scrutiny by the Court. The first is *Kuhn v. Wyeth, Inc*., 686 F.3d 618, 625 (8th Cir. 2012) in which an MDL transferee court was persuaded by the pharmaceutical defendant into doing precisely what Forest urges this Court to do, *i.e.,* to exclude plaintiff's general causation expert and grant summary judgment. In spite of the "abuse of discretion" standard of review, the Eighth Circuit reversed. *Id.* The second opinion is Judge Saris's monumental discourse in *In re Neurontin Mktg., Sales Practices, & Products Liab. Litig.*, 612 F. Supp. 2d 116 (D. Mass. 2009)[10]. This case, and its sequel[11], is important because it involved multiple claims of psychoactive medication induced suicidality. Judge Saris' scholarly opinion, particularly his discussion of the limitations of epidemiological evidence and the value of "adverse event data" (which Forest insists on labeling as "anecdotal case reports") with regard to this rare but tragic phenomenon, are particularly *apropos* with regard to the motion at hand. His ruling: *Daubert* motion denied.

---

[9] One of the earliest opinions explaining the need for caution in balancing *Daubert* gatekeeping with constitutional rights, is the Second Circuit's admonition in *McCulloch v. H. B. Fuller Co*., 61 F.3d 1038, 1045 (2nd Cir. 1995) that "[c]ourts must be especially careful not to hobble the jury system by excluding potentially useful evidence. Prematurely cutting off the flow of evidence to the jury generally favors defendants, who do not have the burden of proof on most issues, leading not only to a violation of the Constitution, but a tilting of the scales of justice."

[10] The undersigned lead trial counsel for plaintiffs in these MDL proceedings has been litigating SSRI-induced suicidality cases since the summer of 1995. Not surprisingly, we have briefed *Daubert* motions similar to this one on dozens of occasions. In early briefing we laid out a few of the basic principles of law under the rubric of "Primer." Happily, that jargon was adopted by Judge Saris in his May 2009 opinion in the *Neurontin* case.

[11] *In re Neurontin Mktg., Sales Practices, & Products Liab. Litig.*, MDL 1629, 2009 WL 3756328, 7 (D. Mass. Aug. 14, 2009).

Argument and Authorities

I. A *DAUBERT* PRIMER.

Any briefing on point should start, of course, with the Supreme Court. Each of the cases in the *Daubert-Joiner-Kumho* triumvirate establish a different, but important point of law. First, with regard to *Daubert* itself, it is important to remember that the pharmaceutical industry *lost* the case. Both Merrell Dow and its pharmaceutical *amici* argued strenuously in the Supreme Court for adoption of the *Frye* standard of "generally accepted" orthodoxy. Obviously, if that were the law, then the industry's very widespread control of clinical trials and academic medicine could result in exclusion of countervailing expert opinions in almost all products liability pharmaceutical cases.[12] But the Supreme Court rejected the industry's approach, choosing instead, to control the "gates" of expert opinion testimony admissibility by focusing on four non-exclusive criteria: "(1) whether the theory or technique applied can be tested, (2) whether the theory or technique has been subject to peer-review or publication, (3) the known or potential rate of error, and (4) whether it is accepted in the relevant discipline." *Kuhn, supra,* 686 F3d at 625 citing *Daubert.* In offering these four factors the *Kuhn* court concluded that "'vigorous cross-examination, presentation of contrary evidence, and careful instruction on the burden of proof, are the traditional and appropriate means of attacking shaky but admissible evidence.'" *Id.* at 625 (quoting *Daubert,* 509 U.S. at 596). *Accord McIntosh v Monsanto Co.,* 462 F Supp 2d 1025, 1032 (E.D. Mo. 2006)(Rejecting challenge to expert)(Sippel, J.); *Giles v. Wyeth*, 500 F.Supp.2d 1048, 1060 (S.D. Ill. 2007)(rejecting similar challenge to expert opinion testimony regarding opinion that antidepressant Effexor causes suicide.)

[12] This is not just pontification from Plaintiff's counsel. The Washington Post has recently highlighted this very problem with published medical literature. *See* http://www.washingtonpost.com/business/economy/as-drug-industrys-influence-over-research-grows-so-does-the-potential-for-bias/2012/11/24/bb64d596-1264-11e2-be82-c3411b7680a9_story.html?hpid=z1.

As will be discussed more fully, Dr. Healy's opinions in this case past muster under all *Daubert* criteria.

After *Daubert* is the often forgotten *Joiner* opinion that underscores the notion that *Daubert* decisions are *discretionary*.[13] In the pharmaceutical litigation process *Daubert* motions are ordinarily dispositive in nature and therefore frequently coupled with a motion for summary judgment. The standard of review for the latter is *de novo*; the standard of review for a *Daubert* exclusionary ruling is discretionary.[14] In spite of this, however, the most recent case from the Eighth Circuit, which is remarkably on point, found the exclusion of plaintiff's general causation expert to be an abuse of discretion. *Kuhn, supra,* 686 F3d at 625. *Kuhn* involved allegations of breast cancer caused by hormone therapy drugs wherein the presiding judge in the MDL was persuaded by the defendant to exclude the plaintiffs' expert on general causation and granting summary judgment. *In re Prempro Products Liab. Litig*., MDL 4:03CV1507-WRW, 2011 WL 768064, 4 (W.D. Ark. Feb. 14, 2011). On July 26, 2012, the Eighth Circuit found that decision to be an abuse of discretion, reversed, and remanded for trials on the merits. *Kuhn,* 686 F3d at 618. It was a 2:1 decision. *Id*. The dissent would have affirmed solely because of the breadth of discretion accorded to the trial judge, even though the import of the ruling was to deny an entire group of plaintiffs in an MDL their day in court. *Id*. at 633. If there is any lesson in this, it is that any court that is faced with the prospect of

---

[13] *General Electric Co. v. Joiner*, 522 U.S. 136 (1997).

[14] The breadth of discretion accorded to trial judges is extremely significant and helpful to an understanding of Forest's almost singular reliance on the Tenth Circuit's opinion affirming Judge Vratil's exclusion of Dr. Healy in the Zoloft/SSRI *Miller* case. *Miller v. Pfizer, Inc.*, 196 F.Supp.2d 1062 (D. Kan 2002), *aff'd.* 356 F.3d 1326 (10th Cir. 2004). Less than a year before that ruling, another federal judge in the Tenth Circuit rejected similar *Daubert* challenges to Dr. Healy in the SSRI murder/suicide case of *Tobin v. Smithkline Beecham*. 164 F.Supp.2d 1278 (D. Wy. 2001). The case was tried, the jury found that "Paxil can cause some people to become homicidal and/or suicidal," and the plaintiff's won. Exhibit 1 at 1. The Tenth Circuit's consideration of that ruling was coopted by a settlement of the case. However, it is highly likely that it would have also sustained Magistrate Judge Beaman's ruling in that case, because in *Hollander v. Sandoz Pharmaceuticals Corp.*, 289 F.3d 1193, 1204, 1206 (10th Cir. 2002), it wrote that "*Daubert's* effort to safeguard the reliability of science in the courtroom may produce a counter-intuitive effect: different courts relying on the essentially the same science may reach different results."

making a *Daubert* ruling that is in fact dispositive, should be constitutionally chary. *See also* FN9, *supra*.

The third case, *Kumho,* is important because of its laser-like focus on the "intellectual rigor" standard, *i.e.,* whether the expert utilizes the same level of "intellectual rigor" in testifying that he/she does in his normal professional activities. *Kumho Tire Co. v. Carmichael*, 526 U.S. 137, 152, (1999). The Eighth Circuit and this Court have both recognized this all important role of the "intellectual rigor" standard, particularly in light of the 2000 amendments and comments to Rule 702. *See e.g., Marmo v. Tyson Fresh Meats, Inc*., 457 F.3d 748, 757 (8th Cir. 2006); *Arnold v. Amada N. Am., Inc.*, 2008 WL 3411789 (E.D. Mo., Aug. 8, 2008).

Both this Court and the Eighth Circuit have dutifully followed and applied the *Daubert/Kumho* standards. The recent Eighth Circuit opinion in *Kuhn, supra,* illustrates the pitfalls. It acknowledged the existence of scientific studies and other literature supporting Wyeth's "contrary position," the limitations of clinical trial data to answer questions of rare side effects,[15] and even contrary testimony by the same expert in other contexts, and yet still noted that "it is not the province of the court to choose between the competing theories when both are supported by reliable scientific evidence." *Kuhn,* 686 F3d at 633.

Finally, before leaving the general principles of law that govern the disposition of *Daubert* motions, and although touched on previously, it is important to focus on a critical procedural distinction between a motion *in limine* of this nature and a motion for summary judgment, that is usually paired with it, although not present in this instance. Under Rule 56, Fed.R.Civ.P., the materials submitted in support of, and in opposition to, summary judgment motions must be "admissible in evidence." But, with regard to the *Daubert*-gatekeeping duties, this is not the case.

[15] *See also* Forest's and the FDA's admission regarding the limitations of clinical trial data found in the companion briefing regarding Dr. Hamrell.

Rule 104, FED. R. EVID., specifically provides that the Court may look to all available information, and, its sole discretion, give each the weight that it deems appropriate. Thus, documents like the Plaintiffs Science Presentation. Exhibits 14 and 15 (DVD and PowerPoint), and government documents, news articles, and other information from reliable sources, may provide a basis for this Court's action on this motion.

In considering these legal standards, there can be little question that Dr. David Healy has shown remarkable consistency in his opinions about SSRI induced suicidality, from his first peer-reviewed publication on this topic in 1991, to his opinions in this case more than two decades later. Because he passes both the "intellectual rigor" standard set out in *Kumho* and *Daubert*, Forest's motion should be denied.

II. SSRI DRUGS AND THE RISK OF SUICIDE – DR. HEALY'S TWO+ DECADES OF CONSISTENT, COURAGEOUS "INTELLECTUAL RIGOR".

If there is any litmus test for admissibility under the Supreme Court's reasoning, it is the two sided *Kumho* coin. On one side, the Court looks to see whether the expert brings the same level of "intellectual rigor" to the courtroom that he/she uses in his normal day job. *Kumho,* 526 U.S. at 152. On the other side, the Court examines the question of whether or not the expert's opinions seem to be "litigation driven."

Happily, in this case, an examination of these factors can, with very little effort, reveal the lack of merit in Forest's motion. Prozac, the first of the SSRI[16] blockbuster drugs, was launched in this country in 1988. By late 1989, a widely publicized work-site massacre had put the issue of SSRI induced violence/suicidality squarely in the public focus.[17] Then, in February 1990, an article by two

---

[16] Selective Serotonin Reuptake Inhibitors. Both Celexa and Lexapro are SSRI drugs.

[17] On September 14, 1989, then 47-year-old Joseph T. Wesbecker, a Prozac user who was on disability for mental illness, entered Standard Gravure, his former workplace, killed eight people and injured twelve more before committing suicide.

highly prominent Harvard neuro-psychopharmacologists, Martin Teicher and Jonathon Cole, gave scientific credibility to the theory, and focused the scrutiny of scientists all over the world on the potential dangers of these seemingly beneficial drugs.[18] Exhibit16 (Teicher et al., *Emergence of Intense Suicidal Preoccupation During Fluoxetine Treatment,* Am J Psychiatry 1990; 147: 207-210).

In 1991, Dr. John Mann and Dr. Anthony Rothschild wrote peer-reviewed papers on this direct point. Dr. Mann explained the biologic plausibility of this phenomenon when he wrote that in a "subset of patients, the introduction of a serotonin reuptake inhibitor or an increase in dose may result in an exaggerated initial decrease in serotonin transmission and, thus, enhance suicidality early in treatment because of an effect on the neurobiologic regulator of suicide or aggression threshold....". Exhibit 17 at 1032 (Mann et al., *The Emergence of Suicidal Ideation and Behavior During Antidepressant Pharmacotherapy*, Arch Gen Psychiatry 1991; 48: 1027-1033). Dr. Rothschild *et al.* confirmed causality with a scientific experiment in a 1991 study that received peer-reviewed publication. Exhibit 18 at 493 (Rothschild et al., *Reexposure to Fluoxetine After Serious Suicide Attempts by Three Patients: The Role of Akathisia*, J Clin Psychiatry 1991:52 :491 - 493). The authors of this peer-reviewed article had treated three patients, all of whom had serious suicide attempts while taking Prozac. *Id*. at 491. Prozac was discontinued (dechallenge) and patients got somewhat better. *Id*. Rothschild and Locke then rechallenged all three with Prozac again. *Id*. Amazingly, all three had the same recurrence of both akathisia[19] and suicidality which they had experienced previously. *Id*. Prozac was removed; the patients again got better. *Id*. Although the

[18] As Forest's expert, Dr. Stahl acknowledges in his report, "the question whether SSRI antidepressants in general can cause a person to become suicidal, attempt suicide, or commit suicide has been of concern for many years, dating as far back as at least 1990 and an article by Teicher and Cole . . ." Exhibit 36 at 27.

[19] The DSM IV describes akathisia as a "sense of inner restlessness...." that may be associated with...suicide attempts." Exhibit 19 at 800-801 (DSM-IV).

Rothschild and Locke study[20] was not "placebo controlled" or blinded, it nonetheless had significant scientific controls and extremely significant findings. It was controlled by virtue of the fact that there were not one, but two different, well-trained clinicians/authors running the study. Its publication in a peer-reviewed journal is another indicium of scientific reliability.

Although Defendant's expert, Dr. Stahl, label the Teicher & Cole article, and the Rothschild & Locke articles that followed it in 1991 as mere "anecdotal case reports,"[21] in fact, Dr. Rothschild (who has subsequently served as an expert for several SSRI manufacturers in suicide cases) summed up his scientific rechallenge experiment with the following unequivocal observation:

> Patients need to be reassured that the overwhelming symptoms being experienced are the side effects of medication and are treatable. Our patients had concluded their illness had taken such a dramatic turn for the worse that their life was no longer worth living.

Exhibit 18 at 493.

To understand the full import of this evidence, one should examine the writings and testimony of a former FDA official who, among other things, has testified as an expert in SSRI suicide cases for the Ulmer Berne firm that is defending Forest in these cases. Her name is Dr. Judith Jones, and, in a deposition in another case, Dr. Jones was asked to analyze the Rothschild & Locke paper, which she had cited in her report, using the "FDA Causality Algorithm" about which she herself had written and published in a peer-reviewed journal. Exhibit 22 (Jones, *Adverse Drug*

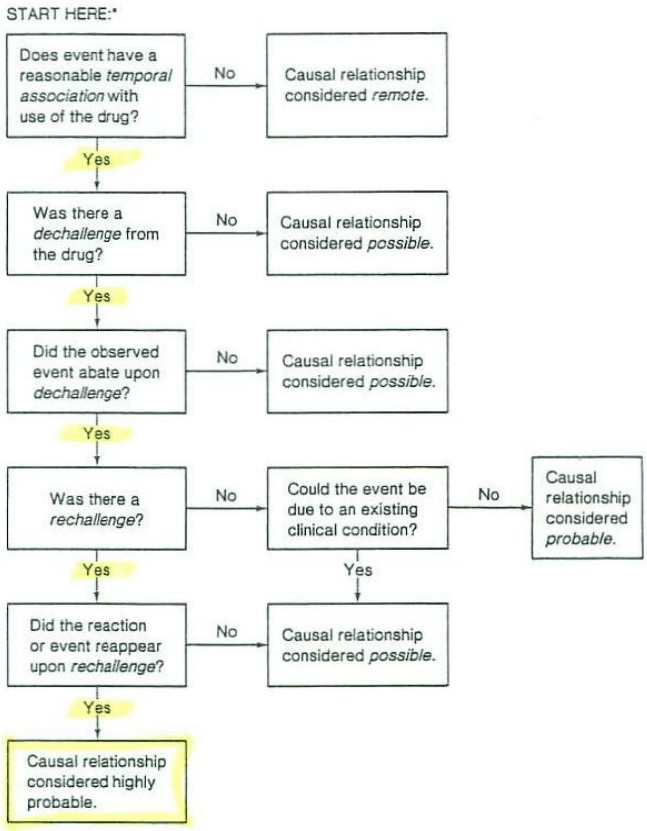
---

[20] In his role as a Lilly-paid expert, Dr. Rothschild has taken umbrage at the word "study" to describe his endeavor. However, Dr. Rothschild has used this very word, three times, and under oath, to describe his paper. Exhibit 20 at 42:19-24, 43:1-12, 44:8-18 (Rothschild Deposition dated 08.09.05)[FILED UNDER SEAL].

[21] Dr. Stahl's opinions that minimize the importance of case reports runs completely contrary to the importance both Forest and FDA place upon them. *"[S]afety signal* refers to a concern about an excess of adverse events compared to what would be expected to be associated with a product's use. Signals can arise from postmarketing data and other sources, such as preclinical data and events associated with other products in the same pharmacologic class. It is possible that even a single well documented case report can be viewed as a signal, particularly if the report describes a positive rechallenge or if the event is extremely rare in the absence of drug use." Exhibit 21 at 4 (2005 FDA Guidance for Industry) (emphasis in original)

Reactions in the Community Health Setting: Approaches to Recognizing, Counseling, and Reporting, Family Community Health 1982, 5:58 - 67). The result, as demonstrated graphically below, was an overwhelming "highly probable" causal relationship:

FDA Causality Algorithm



*Each drug is carried through independently; if > 1 drug was dechallenged or rechallenged simultaneously causality for all is ≤ possible.

QUESTIONS:

1. Did the reaction follow a reasonable temporal sequence?
2. Did the patient improve after stopping the drug?
3. Did the reaction reappear on repeated exposure (rechallenge)?
4. Could the reaction be reasonably explained by the known characteristics of the patient's *clinical state*?

Fig 2. Algorithm for establishing causal relationship between drug and event, used by FDA's Division of Drug Experience.

Id. at 62, Figure 2. While Plaintiff appreciates the above is based on only three case reports, the significance of this result should not be overlooked by the Court in it's *Daubert* analysis. For the FDA itself recognizes that "even a single-well documented case report can be viewed as a signal,

particularly if the report describes a positive rechallenge or if the event is extremely rare in the absence of drug use." Exhibit 21 at 4.[22]

On the other side of the pond from Drs. Teicher, Cole, Rothschild and Locke, Dr. Healy and his colleagues, Drs. Creaney and Murray, published a similar article in 1991. Exhibit 23 (Healy and Creaney, *Antidepressant Induced Suicidal Ideation*, Human Psychopharmacology, Vol. 6, 329-332 (1991). Healy was the junior author on the paper, which contained a report on two cases of apparent SSRI induced suicidality, and concluded that there are "two sorts of side effects of psychotropic compounds" one of which is "increased nervousness and restlessness and dissociative reactions" that could lead to, and explain, treatment emergent suicidality. *Id*. at 332. Three years later, in 1994, Dr. Healy was the sole author of another peer-reviewed article entitled "The Fluoxetine and Suicide Controversy: *A Review of the Evidence*."Exhibit 24 (Healy, *The Fluoxetine and Suicide Controversy*, CNS Drugs 1994:1(3);223-31 (1994)). Unlike the other papers listed herein, this one was a scientific, analytical review of all of the extant evidence at that time. This publication came out three years before Dr. Healy ever appeared as an expert in any civil litigation in this country.

The following points made by Dr. Healy in that article are fully consistent with his opinions, 18 years later, in this litigation:

- The February 1990 article by Teicher & Cole "suggested that these agents somewhat perversely *cause suicide fatalities"*

- A reanalysis of clinical trial data used by Eli Lilly to downplay the potential causality actually "can be interpreted such that fluoxetine does indeed lead to the emergence of suicidal ideation."

-- Because the clinical trials were not designed to measure incipient suicidality, "the use of sophisticated postmarketing surveillance is the only accurate way

[22] A "signal" refers to a concern about an excess of adverse events. *Id.*

of assessing the possibility of suicidal ideation induced by the newer agents."[23]

-- There is a recognized relationship between lower levels of the serotonin metabolite, 5-HIAA and suicidality. [Note: SSRI's actually lower 5-HIAA.]

-- Although there is a concern that case reports can be an "unreliable form of information," in this arena, there is a "broad correspondence" among them, there is a large "volume of case reports and other studies [that] is sufficient to demonstrate that antidepressants and antipsychotics may induce suicidal ideation in certain individuals," "some of the case reports . . . do appear sufficiently well documented and detailed to sustain an argument that fluoxetine may lead to the emergence of suicidal ideation" and, at least two, *i.e.,* Rothschild and Creaney showed positive dechallenge/rechallenge evidence, which is a compelling indicator of causality

-- The most plausible mechanism to explain treatment emergent suicidality in most SSRI cases is via the production of "akathisia" or an akathisia-like "agitation or dysphoria" AND

-- The evidence from multiple sources shows that "the time of emergence of suicidal ideation" is "about 10 to 14 days after initiation of fluoxetine treatment."[24]

Id. at 225-229. At the time this peer-reviewed article was published, Dr. Healy had no civil litigation experience to report as a potential conflict of interest. Indeed, ironically, the only such statement he made in the article was that "Dr. Healy acts as a consultant for Eli Lilly" (the manufacturer of Prozac/fluoxetine). *Id.* at 230.

In the 18 years since this article was published, the evidence has continued to accumulate, and Dr. Healy has continued to publish articles[25] about it and to give speeches before international scientific audiences about the potential of SSRI's to precipitate suicidality, not only in children like

---

[23] This observation is, of course, fully consistent with the opinions and methodology of Dr. Hamrell.

[24] *See* Exhibit 25 (Lexapro MDL Clients Chart).

[25] For example, his 2003 "*Lines of Evidence*" paper focused on clinical trial data and pointed out, among other things, that there was a "doubling" of the risk of suicidality and a demonstrable "dose dependent" link between SSRI's and suicidality and akathisia. Exhibit 26 at 71-72, 77 (Healy, *Lines of Evidence on the Risks of Suicide with Selective Serotonin Reuptake Inhibitors*, Psychother Psychosom 2003:72:71-79). Dose dependency is another scientifically accepted indicium of a drug side effect.

Matthew Miller, but also in adults – particularly in the "peak time . . . shortly after the individual start treatment" with an SSRI. Exhibit 24 at 229. His 1994 opinions have been confirmed by closer examination of all the available SSRI clinical trial data, to include the clinical trial data for Celexa and Lexapro.[26]

Moreover, since early 2005, the FDA has mandated a **BLACK BOX WARNING** to "patients of all ages" about the risk of treatment emergent suicidality, and its precursor conditions like akathisia. Here is what the current Lexapro boxed warning states:

WARNINGS: SUICIDALITY AND ANTIDEPRESSANT DRUGS

Antidepressants increased the risk compared to placebo of suicidal thinking and behavior (suicidality) in children, adolescents, and young adults in short-term studies of major depressive disorder (MDD) and other psychiatric disorders. Anyone considering the use of Lexapro or any other antidepressant in a child, adolescent, or young adult must balance this risk with the clinical need. Short-term studies did not show an increase in the risk of suicidality with antidepressants compared to placebo in adults beyond age 24; there was a reduction in risk with antidepressants compared to placebo in adults aged 65 and older. Depression and certain other psychiatric disorders are themselves associated with increases in the risk of suicide. Patients of all ages who are started on antidepressant therapy should be monitored appropriately and observed closely for clinical worsening, suicidality, or unusual changes in behavior. Families and caregivers should be advised of the need for close observation and communication with the prescriber. Lexapro is not approved for use in pediatric patients less than 12 years of age. *[See Warnings and Precautions: Clinical Worsening and Suicide Risk (5.1), Patient Counseling Information: Information for Patients (17.1), and Used in Specific Populations: Pediatric Use (8.4)]*.

Exhibit 28 at 3 (May 2011 Lexapro Label). Notably, the FDA has admonished that "Patients ***of all ages who are started on antidepressant therapy*** should be monitored appropriately and observed closely for clinical worsening, suicidality, or unusual changes in behavior." *Id* (emphasis added).[27]

---

[26] The paper by *Fergusson*, *et.al*. that Dr. Healy coauthored, examined evidence from hundreds of SSRI clinical trials, including those for Celexa, and found a statistically "significant increase in the odds of suicide attempts" that was more than double the similar risk for patients taking placebos. Exhibit 27 at 1 (Fergusson, *et al.*, *Association between suicide attempts and selective serotonin reuptake inhibitors: A systematic review of randomized controlled trials*, BMJ 2005; 330, 396-399).

[27] Further in the label, the warning, yet again, provides: "***All patients*** being treated with antidepressants for any indication should be monitored appropriately and observed closely for clinical worsening, suicidality, and unusual changes in behavior, especially during the initial few months of a course of drug therapy, or at times of dose changes, either increases or decreases. " *Id*. at 5 (emphasis added).

FDA has also recognized that, paradoxically, SSRI drugs may trigger violent suicidality for some individual, vulnerable patients during the "peak time" when the patients first start the drug or alters their dosing, and, yet, with regard to the entire population of patients as a whole, it may be benign with regard to this particular side effect. In its November 6, 2006, Memorandum, the FDA published the results of its Columbia Study Group Reclassification and discussed this seemingly paradoxical side effect. Exhibit 29 (2006 PDAC Memo). In the Memorandum itself, the FDA noted that, if one looked at older patients, like some of those involved in these MDL proceedings, then the data suggest that, for those who were able to tolerate the medication, it would, in the long run, have a slightly protective effect *vis-à-vis* suicidality. *Id*. at 5.

And, yet, paradoxically, the FDA also cited a peer-reviewed epidemiological article that documents a nearly fivefold increase in the risk of violent, completed suicides by a few "vulnerable" elderly patients in the early period of drug therapy. *Id.* at 5. FDA explained that this seeming contradiction was, in fact, no contradiction at all:

> "In fact, the dual findings of an early increase in the risk of suicidality but also a longer-term benefit with antidepressant treatment would, if both true, not necessarily be inconsistent. It is quite possible for a drug to have opposite effects over time, even within the same domain."

Id. at 2.

The Juurlink article, cited by the FDA for this "paradox" warrants further mention. Exhibit 30 (*Juurlink*, et al., *The Risk of Suicide With Selective Serotonin Reuptake Inhibitors in the Elderly*, Am J Psychiatry, 163:5 May 2006). This study was a large scale epidemiological study focused on older patients, *i.e.,* the ones that Forest argues are actually *protected* with respect to suicidogenicity by Celexa/Lexapro. *Id*. at 813. Therein, the authors found, with **statistically significant** results, that if one looks solely at the first four weeks of drug therapy, there is a 4.8x risk of *violent suicide* for

patients in this age group taking an SSRI . *Id*. at 813, 816. This study specifically included Celexa data. *Id*. at 814.

There are 12 patients involved in the remaining MDL cases. Exhibit 25. The shortest period of time for any of them between drug initiation or dosage increase to suicide was Leon Cross at three days. *Id*. at 1. The longest period of time between drug initiation or dosage increase to suicide was Brian Oliver, who stayed on the drug for 45 days.[28] *Id*. at 2. The average is 15 days.

Most astonishing, however, is the fact that, in 2007, *after* the patent for Prozac had expired, Eli Lilly's own scientists, who had been swearing for years that Prozac did not cause anyone to become suicidal, acknowledged in a peer-reviewed, published paper that SSRI's *do* cause a small subset of vulnerable patients to become suicidal, especially during the early period of their SSRI therapy. Exhibit 31 (Perlis et al., *Treatment Associated Suicidal Ideation and Adverse Effects in an Open, Multicenter Trial of Fluoxetine for Major Depressive Episodes*, Psychother Psychosom 2007; 76:40-46). Here is what the authors, including Lilly's own Dr. Beasley, stated:

> "Consistent with a previous analysis of suicidal behavior, the majority of new [suicidal ideation] emerged within the first 4 weeks, with the greatest incidence in the first week. This result suggests that the initial 4-week treatment period is one where vigilance is particularly important. On the other hand some additional [suicidal ideation] emerged later in the study, indicating that individuals remain vulnerable to emergence of [suicidal ideation] after the initial month..Indeed, antidepressants are known to precipitate [conditions leading to suicide] in a small subset of vulnerable patients"

Id. at 40, 44.

[28] For clarity ,Bruce Muzichuck had been on Lexapro for six months, when his dosage was doubled. *Id*. at 2. He committed suicide 23 days later.

The bottom line for purposes of this motion is that the overwhelming evidence[29] cited by Dr. Healy in his report and his deposition, and confirmed by other corroborating information, as permitted by Rule 104, FED. R. EVID., demonstrates that Healy's opinion regarding general causation pass the "intellectual rigor" test. To be sure, Forest's motion papers demonstrate that it has fodder for cross examination, but, as the *Daubert* Court itself explained, that is the "traditional" and preferred way to address adverse expert testimony. Forest's motion should be denied.

III. DR. HEALY'S OPINIONS ARE BOTH RELEVANT AND RELIABLE WITHIN THE MEANING OF RULE 702 AND *DAUBERT*.

In addition to passing the "intellectual rigor" test of *Kumho*, Dr. Healy's opinions also pass muster under all four *Daubert* criteria: His opinions regarding SSRI induced akathisia and suicidality have been published in numerous peer-reviewed articles by him, and have been corroborated by extensive scientific literature by others. At this point in time, they have clearly achieved "general acceptance," as evidence by (a) the FDA mandated **BLACK BOX WARNINGS**,[30] (b) the DSM-IV-TR, section 333.99,[31] and (c) the host of scientific evidence cited in Healy's report and deposition. Although Lilly never conducted the "rechallenged protocol" it promised to do in order

---

[29] Citations to all of the scientific literature on point could go on and on and on. For those more inclined towards sophisticated Bayesian probabilistic modeling, the Aursnes paper, might be more persuasive. Exhibit 32 (Aursnes et al., *Suicide attempts in clinical trials with paroxetine randomised against placebo*, BMC Medicine 2005, 3:14;1-5). This meta-analysis of SSRI clinical trial data was published in a peer-reviewed article in which the authors were granted access to previously unpublished data. Using a Bayesian approach to causality determination, these authors examined SSRI clinical trial data from the late 1980's. While taking a "more conservative approach" in measuring outcomes, their statistical analysis revealed that adults taking antidepressants have an increased risk of suicidality in the short term. *Id.* at 1, 5.

[30] In fact, the current FDA approved warnings caution caregivers to expressly be on the look out for akathisia, and signs thereof, and to call a doctor or 911 immediately if experienced: " The following symptoms, anxiety, agitation, panic attacks, insomnia, irritability, hostility, aggressiveness, impulsivity, akathisia (psychomotor restlessness), hypomania, and mania, have been reported in adult and pediatric patients being treated with antidepressants for major depressive disorder as well as for other indications, both psychiatric and nonpsychiatric." Exhibit 28 at 5, 23.

[31] Section 333.99 thereto expressly provides that akathisia may be associated with dysphoria, irritability, aggression, or suicide attempts. Exhibit 19 at 800-801.

to test the hypothesis that Prozac causes suicide on a wide-scale basis,[32] the existent dechallenge/rechallenge evidence from Rothschild and others is strong corroboration of an SSRI induced side effect. And, finally, the "statistically significant" evidence that Healy cites in his peer-reviewed writings and his report in this case is within the norms of "rates of error" as measured by "p-values" and "confidence intervals."

A. Healy's Opinions Are "Generally Accepted". *IF* the pharmaceutical industry had won *Daubert*, "general acceptance" would be the only test. And, yet, Healy would easily pass it . As Judge Ambrose wrote in her 2002 opinion in the *Cassidy* case, she was "willing to accept that his [Dr. Healy's] theory has attended general acceptance in the relevant scientific community." Exhibit 4 at 10. If this was true in 2002, then the ten years from then until now, including an extensive **BLACK BOX** warning regarding this issue, have done nothing but strengthen Judge Ambrose's claim.

First, there is no room for dispute whatsoever that the FDA has concluded that SSRI drugs, including both Celexa and Lexapro can *cause* suicidality in children and adolescents, 25 and under. In its May and July 2005 Public Health Advisories for all SSRIs, including Celexa and Lexapro, the FDA states that children and adolescents become suicidal "due to drug." Exhibit 9 at 1; Exhibit10 at 1. The FDA made crystal clear that this related to "any type of antidepressant" including Lexapro and Celexa. *Id.*[33]

Moreover, it is also important to note that the FDA treats the SSRI antidepressants as a class. Exhibit 29 at Tables 15-16. They do so because they all have a similar mechanism of action as well

---

[32] Exhibit 33 (Beasley Protocol); Exhibit 34 at 85:9-14; 90:12-91:9 (Beasley deposition in *Espinoza*)[FILED UNDER SEAL].

[33] This public health advisory was released. However, once the pharmaceutical industry saw it, they were able to successfully negotiate with the FDA to have it removed.

as similar side effect profiles. *Id.* To that end, the FDA, in a similar manner to Dr. Healy's peer-reviewed publications, has aggregated the data amongst all SSRI's and antidepressants when it examines this issue. *Id*. at 26. It does so because these types of side effects are rare events. *Id.* The FDA found that of the six SSRIs analyzed, Lexapro had by far and away the highest risk of suicidal behavior verse placebo, with an odds ratio of 5.67 that was borderline statistically significant (95% CI .94-32.4, p-value .06). *Id*. With regard to suicidality risk, both Lexapro (2.44; 95% CI .90-6.63; p-value .08) and Celexa (2.11; 95% CI .90-4.94; p-value .08) users had borderline statistically significant increased risk as compared to placebo. *Id*. at 24.[34]

Although Forest chides Dr. Healy on pages 12-14 for not "connecting up" his exploration of the history of the development of Celexa and Lexapro, it is they who lose sight of the significance of this review. Like the FDA, in his report Dr. Healy explains the similar safety profiles of the two sister drugs, their biochemistry (pages 14-15), a comparison of the clinical drop-out rates for both medications (pages 16-17), the biases in the published literature regarding these two products (page 41), and how the pharmacology of the medications does not support the marketing message (pages (43-45). Although, not yet ripe for the Court's determination, clearly Forest's marketing activities regarding these medications and whatever effect it had on prescribing physicians is highly relevant to the matters at hand.

Another one of the "generally accepted" ways that medical scientists determine causation is by reference to the 19th Century "Koch's Postulates" which were utilized by the United States Surgeon General in 1964 to assess the relationship between smoking and lung cancer and subsequently appropriated in 1965 by the Father of Modern Epidemiology, Sir Austin Bradford-Hill

[34] With respect to the risk suicidality, the FDA found the risk posed by Celexa to be 2.11 (95% CI .9-4.94) and Lexapro to be 2.44 (95% CI .90-6.63). Although these two numbers did not achieve statistical significance, the need not do so to remain important scientific evidence. *Matrixx, infra*. Nevertheless, the narrow confidence intervals speaks to the reliability of the results from a statistical perspective.

for that nascent field of scientific endeavor. REFERENCE MANUAL ON SCIENTIFIC EVIDENCE: THIRD EDITION, *Reference Guide on Epidemiology*, Section V at 375-76 (National Academies Press, 2011)[hereinafter "*Reference Guide*"].[35]

As Forest's expert, Dr. Concato acknowledges in his report in this case, these factors are "formal criteria for causation." Exhibit 35 at 25-26 (Concato Report). Dr. Concato's report further observes that, although Healy's "Rule 26 Report is not organized using these categories," one can evaluate Dr. Healy's report with regard to them. *Id*. Forest's psychopharmacology expert, Dr. Stahl, agrees, describing "the requirements of and use of the Bradford-Hill criteria, to assess causation." Exhibit 36 at 22. He adds that these methods "are the standard and generally accepted methods in my field." *Id*. Analysis of Dr. Healy's opinions, using these "general accepted" criteria, reflects that they are amply sufficient.

Of the nine Bradford Hill criteria, Dr. Concato only criticizes Dr. Healy's report with regard to two, *i.e.,* replication of findings and consideration of alternative explanations. Exhibit 35 at 26. Dr. Healy's response to those criticisms is contained in the attached, Supplemental Declaration. Exhibit 37 at 1-2 (Healy Declaration). First, with regard to the criticism that he did not considering alternative explanations, Dr. Healy responds: " I absolutely did consider alternative explanations, to include results from randomized trials and observational studies suggesting a beneficial SSRI-suicide association in adults but I disagree with Dr. Concato's interpretation of evidence. I do so particularly because of my knowledge that pharmaceutical companies have miscoded suicidal events

---

[35] There are nine of these so-called "Bradford-Hill" factors: (1) temporal relationship; (2) strength of the association; (3) dose-response relationship; (4) replication of the findings; (5) biologic plausibility (coherence with existing knowledge); (6) consideration of alternative explanations; (7) cessation of exposure [often described as "dechallenge" or "rechallenge"]; (8) specificity of the association; and (9) consistency with other knowledge. *See In re Neurontin Mktg., Sales Practices, & Products Liab. Litig.*, 612 F. Supp. 2d 116, 132 (D. Mass. 2009)(Recognizing, discussing, and applying Bradford Hill criteria in *Daubert* inquiry.). "***These factors are viewed as guidelines, and it is acknowledged that each factor need not be fulfilled in order for a researcher to proclaim causation.***" *Id*. (emphasis added).

to conceal the problems of suicide and my own peer-reviewed research. See Page 16, 17, and 47 of my report." *Id*. at 1. With regard to the second Bradford Hill criticism that Dr. Healy's report"does not appear to acknowledge that beyond isolated case reports (per Dr. Healy and several other authors), the detection of suicide-related events among healthy volunteers has not been established in adults—nor that evidence is available to contradict mechanisms, such as emotional blunting….", Dr. Healy responds in part that it is now clear that there have been several suicides of healthy volunteers in a number of SSRI healthy volunteer trials. See my report pages 18-23." *Id*. at 2.

What Dr. Concato does not address in his report is the fact that, as Dr. Healy's report reflects, most of the other Bradford-Hill factors militate strongly in favor of Healy's general causation opinions. First, there is a strong temporal relationship between the patients' ingestion of SSRI drugs and the development of suicidality. Exhibit 16 at 207; Exhibit 18 at 491; Exhibit 23 at 329. The current warning information itself reflects this phenomenon. Exhibit 28 at 1. Second, the clinical trial and epidemiological data show a very strong association. This is typically measured in terms of relative risk or odds ratios, and, as Dr. Healy has shown, there is a statistically significant association of 2.0+ in numerous studies and publications. These include Exhibit 13 at 26, 31; Exhibit 26 at 331; Exhibit 38 at 164-65 (Healy et al., *Antidepressant drug use & the risk of suicide,* International Review of Psychiatry, June 2005; 17(3): 163–172); Exhibit 30 at 813; Exhibit 39 at 216 (Jick *et al.*, *Antidepressants and Suicide*, BMJ. 1995 Jan 28;310(6974):215-8). Even Forest admits there is an epidemiological association found in the scientific community related to Lexapro/Celexa and suicidal events. Exhibit 40 at 2 (Boerstoel email dated 08.12.09)[FILED UNDER SEAL]. Third, the data on Celexa/Lexapro and the other SSRI's show a clear dose-response relationship, which is the hallmark of causality. Exhibit 13 at 16, 20, 24 Fourth, there is biologic plausibility, by virtue of the drugs' affect on the serotonin system, and that system's very clear relationship to

suicidality. *Id*. at 35-37.[36] Fifth/Sixth, the association reflected in numerous publications is both specific and consistent with other knowledge. These include Exhibit 26 at 331; Exhibit 38; Exhibit 30 at 813; Exhibit 39 at 216. Seventh, the dechallenge/rechallenge evidence, like that contained in the Rothschild study way back in 1995, show strong evidence of causality. Exhibit 16 at 207; Exhibit 18 at 491; Exhibit 23 at 329.[37] And eighth, despite Concato's observations, there is a strong replication in the data, across all of the SSRI class of drugs as seen in the cited peer-reviewed literature. Finally, although Dr. Healy did consider it, the "consideration of alternative explanations" factor is one that is most appropriately addressed on a patient by patient basis, in the context of an opinion on specific – not general – causation.

The *Reference Guide* is very careful to point out that it is not necessary to show that all of the Bradford-Hill factors militate in favor of an inference of causation. "One or more factors may be absent, even when a true causal relationship exists." *Id*. at 375.[38] Moreover, it further cautions that "the drawing of causal inferences is informed by scientific expertise, it is *not* a determination that is made using scientific methodology." *Id*.

B. Healy's Opinions Are Published in Peer-reviewed Literature and Based as well on Peer-reviewed Literature from Others. As noted above, not only does Dr. Healy base his opinions on a wealth of peer-reviewed published, literature, but also, he himself has published extensively – both before and after becoming a witness in civil litigation – about the dangers of SSRI

---

[36] *See also* Exhibit 17 and the biological explanation at page 10, *supra.*

[37] As does the application of the data from the Rothschild and Lock paper on Dr. Jones FDA causality algorithm, page 13, *supra,* and the dechallenge/rechallenge data found in postmarketing adverse event reporting identified by Dr. Hamrell. *See* Plaintiff's Response in Opposition to Forest's Motion to Exclude Dr. Hamrell.

[38] Bradford-Hill was careful, himself, way back in 1965 to acknowledge that "none of my nine viewpoints can bring indisputable evidence for or against the cause-and-effect hypothesis and none can be required as a *sine qua non*." A. Bradford-Hill, *The Environment and Disease: Association or Causation?*, 58 Proc. Royal Soc'y Med. 295 (1965), quoted in *Reference Manual* at p. 376n.113. *See also Neurontin, supra*, 612 F.Supp. at 132; FN 34.

induced suicidality. These include the already discussed Exhibit 23; Exhibit 26; Exhibit 38.[39] He has also subjected his views on this topic to the critiques of his peers in numerous international lectures for many years. Dr. Healy does not say one thing in Court, and another in professional circles. A sample of additional peer-reviewed, on point, publications by Dr. Healy are attached for the Court's consideration. Exhibit 41 (Healy et al., *Suicide in the Course of the Treatment of Depression*, Journal of Psychopharmacology 13: 94-99 (1999); Exhibit 42 (Healy, *A failure to warn*, International Journal of Risk & Safety in Medicine, 151-156 (1999); Exhibit 43 (Healy, *Emergence of antidepressant induced suicidality*, Primary Care Psychiatry, 6, 23-28 (2000); Exhibit 44 (Healy *et al.*, *Antidepressants and Suicide: Risk-Benefit Conundrums*, J Clin Neurosci, 28(5):3331-337; Exhibit 45 (Healy et al., *Antidepressants and violence: Problems at the interface of medicine and law*, PLoS Medicine 3, Sept, DOI: 10.1371/journal.pmed.0030372 (2006); Exhibit 46 (Healy, *The Antidepressant Tale: Figures Signifying Nothing?*, Advances in Psychiatric Treatment 12, 320-328 (2006); Exhibit 47 (Healy, *Did regulators fail over selective serotonin reuptake inhibitors*, BMJ 333, 92- 95 (2006). We apologize to the court for the length or exhibits, but this is only a sample of Dr. Healy's peer-reviewed publication on this topic. Even a cursory review of his *C.V.* will reveal this. Exhibit 48 at 9-20 (*Curriculum Vitae* of David Healy, M.D.).

C. Healy's Opinions are Both Testable and Tested. With regard to the "tested or testable" criterion of *Daubert*, we have cited numerous articles written by Dr. Healy and others that have supported the contention that these drugs can lead to akathisia, emotional blunting, psychotic decompensation, and suicide. Dr. Healy discusses several of the studies that support his contention in his report. Exhibit 13 at 35-37.

[39] This peer-reviewed publication expressly included Celexa clinical trial data.

As an aside, we can, without belaboring the point, demonstrate to the Court that the only one really capable of testing the hypothesis that Lexapro and Celexa can cause suicide or suicidality in a large scale manner is Forest and they have not done so. As an example Eli Lilly drafted a protocol to test this hypothesis in 1991, Exhibit 33 [FILE UNDER SEAL], that it promised the FDA that it would do this test, and that it never did. Exhibit 34 at 85:9-14; 90:12-91:9 [FILE UNDER SEAL]. Similarly, Forest has not done appropriate testing to determine if their drugs cause suicide or suicidality. Given the rarity of the event, clinical trials that are not specifically powered to examine this very issue will undoubtably fail to pick up "statistically significant" data due to statistical limitations.

D. The "Rate of Error" on Publications and Computations Healy Uses Is Within Scientific Norms. The REFERENCE MANUAL ON SCIENTIFIC EVIDENCE: THIRD EDITION, *Reference Guide on Epidemiology* considers several different methods of computing error rates. Perhaps the most easily understood are confidence intervals:

> **confidence interval.** An estimate, expressed as a range, for a parameter. For estimates such as averages or rates computed from large samples, a 95% confidence interval is the range from about two standard errors below to two standard errors above the estimate. Intervals obtained this way cover the true value about 95% of the time, and 95% is the confidence level or the confidence coefficient.

Id. at 284-85. By way of example, the previously cited *Fergusson* study coauthored by Dr. Healy found "a significant increase in the odds of suicide attempts (odds ratio 2.28, 95% confidence 1.14 to 4.55 number needed to treat to harm 684) was observed for patients receiving SSRIs compared with placebo." Exhibit 27 at 1. The p-value here was .02. *Id.* at 4. Thus, the result shows that 95% of the time there would be an increased risk of suicide attempts from 14% to at much as 4.5 times for those taking SSRI compared with placebo. Similarly, the *Jink* study found people who received high doses of antidepressants and those who had a prescription in the 30 days before they committed

suicide were also at higher risk than those who had received low doses and had their prescriptions 30 or more days previously (relative risk = 2.3, C.I.1.4 to 3.7 and 2.3, C.I. 1.6 to 3.4) respectively. Exhibit 39 at 215. These results were calculated utilizing a 95% confidence interval. *Id.* Therefore, 95% of the time the true value for persons who committed suicide were on high doses of antidepressants somewhere between 40% to more than 3.5 times more than those on low dose antidepressants. Likewise, persons who committed suicide were somewhere between 60% and 3.5 times more likely to have been on the drug for less than 30 days as opposed to more than 30 day. Other studies, including those written by Dr. Healy, have used this same 95% confidence interval. Exhibit 13 at 26, 31; Exhibit 26; Exhibit 38; Exhibit 30. Thus the known error rate for many of these peer-reviewed studies and Dr. Healy's analysis is both low and known.

IV. EPIDEMIOLOGICAL "STATISTICAL SIGNIFICANCE" IS LEGALLY UNNECESSARY, BUT SCIENTIFICALLY PRESENT IN THIS CASE.

A. The Law: The Supreme Court has ruled: " a lack of statistically significant data does not mean that medical experts have no reliable basis for inferring a causal link between a drug and adverse events.[40] This language, admittedly taken from a federal securities case (and not a *Daubert*) opinion, has been subsequently adopted by federal courts in the pharmaceutical *Daubert* context. For example, in the Chantix MDL the court stated:

> "While the defendant repeatedly harps on the importance of statistically significant data, the United States Supreme Court recently stated that [a] lack of statistically significant data does not mean that medical experts have no reliable basis for inferring a causal link between a drug and adverse events .... medical experts rely on other evidence to establish an inference of causation. *Matrixx Initiatives, Inc. v. Siracsano*, —— U.S. ——, ——, 131 S.Ct. 1309, 1319, 179 L.Ed.2d 398 (2011). The Court further recognized that courts "frequently permit expert testimony on causation based on evidence

[40] *Matrixx Initiatives, Inc. v. Siracusano,* —— U.S. ——, ——, 131 S.Ct. 1309, 1319, 179 L.Ed.2d 398 (2011). Although *Matrixx* was a securities case, as the Court will soon see, recent pharmaceutical cases have cited it in support of their rejection of the "statistical significance" *shibboleth* in products liability cases.

> other than statistical significance. *Id*; citing *Wells v. Ortho Pharmaceutical Corp.,* 788 F.2d 741, 744–745 (11th Cir.1986). Hence, the court does not find the defendant's argument that Dr. Furberg "cannot establish a valid statistical association between Chantix and serious neuropsychiatric events" to be a persuasive reason to exclude his opinion, even if the court found the same to be true. *See* defendant's memorandum (doc. 584) at 13.

"*In re Chantix (Varenicline) Products Liab. Litig.*, 2:09-CV-2039-IPJ, 2012 WL 3871562 (N.D. Ala. Aug. 21, 2012)(quoting *Matrixx* at 319)(internal quotes omitted). The court overseeing the Phen Fen MDL had a similar holding in its *Daubert* analysis of the plaintiffs' expert witnesses:

> "*Daubert* does not require that an expert opinion regarding causation be based on statistical evidence in order to be reliable. *Matrixx Initiatives, Inc. v. Siracusano*, —— U.S. ——, ——, 131 S.Ct. 1309, 1319, 179 L.Ed.2d 398 (2011). In fact, many courts have recognized that medical professionals often base their opinions on data other than statistical evidence from controlled clinical trials or epidemiological studies. *Id.* at 1320. Our Court of Appeals has stated, "we do not believe that a medical expert must always cite published studies on general causation in order to reliably conclude that a particular object caused a particular illness." *Heller,* 167 F.3d at 155."

In re Diet Drugs (Phentermine/Fenfluramine/Dexfenfluramine) Products Liab. Litig., MDL 1203, 2012 WL 3776692 (E.D. Pa. Aug. 30, 2012) (citing *Matrixx Initiatives, Inc. v. Siracusano*, 131 S. Ct. 1309, 1320, (2011); *Heller v. Shaw Indus., Inc.*, 167 F.3d 146, 155 (3d Cir. 1999)).

B. The Science. To understand Forest's focus on epidemiological evidence and the concept of "statistical significance" it is necessary to outline what epidemiology can and cannot do. Fortunately, the Court is not without objective guidance. The 2011 federal REFERENCE MANUAL OF SCIENTIFIC EVIDENCE, *Reference Guide on Epidemiology*, (3rd Edition, 2011) is an invaluable tool. First, we must understand that the field of epidemiology is not designed to address specific causation of any disease process in any individual patient. Rather, "epidemiology is the field of public health and medicine that studies the incidence, distribution, and etiology of disease in human

populations. *Id*. at 335 (emphasis added). Because the focus is on a population at large, it is not surprising that it is not particularly helpful in determining specific causation:

> Epidemiology is concerned with the incidence of disease in populations and *does not address the question of the cause of an individual's disease.*. This question, sometimes referred to as specific causation, is *beyond the domain of the science of epidemiology*. . . . epidemiology addresses whether an agent can cause a disease, not whether an agent did cause a specific plaintiff's disease.

Id. at 382 (Emphasis added).

Nor, indeed, does epidemiology "objectively" prove general causation. Rather, epidemiology provides a framework for a causality assessment that is always, one of *subjective* professional judgment by a qualified expert.

Even with regard to the topic of general causation, there are definite limits regarding what epidemiology can or cannot show. The field originated in circumstances where there was usually one cause of a disease or harm. In those circumstances, the process of attributing risk, excluding alternative possibilities, etc., that is inherent in the science of epidemiology, can be very helpful. But when the adverse event is one that is, almost by definition multifactorial, like suicide (involved in the *Neurontin* case, *supra* and herein, then the problem becomes exceedingly more complex. A drug can contribute in a material way, or, as most states require, be a "substantial factor" in the development of a disease state or adverse event, even though other factors, like age, genetics, preexisting disease state, or other medications may also contribute. But in most states, juries are regularly instructed that "there may be more than one cause present to produce an injury, and more than one person legally responsible for an injury. The plaintiff does not have to prove that the defendant's product was the only or predominant cause of the injury.

As the *Reference Guide* states, "epidemiology cannot objectively prove causation; rather, causation is a *judgment* for epidemiologists and *others* interpreting the epidemiologic data."

Reference Guide at 374. Moreover, "[m]ost researchers are *conservative* when it comes to assessing causal relationships, *often calling for stronger evidence* and more research before a conclusion of causation is drawn." *Id*. In the experience of the undersigned, this is particularly true of those researchers who are employed by pharmaceutical companies. They almost never use the "c" word, *i.e.,* "causality" when referring to any adverse side effect of their company's medication. So unpalatable is this word, that Dr. Joseph Camardo[41] was even hesitant to use it in talking about the *beneficial* effects for which the drug is marketed:

> Q Incidentally -- don't take this wrong, I'm not fussing at you -- but when we're talking about words that you don't like to use, one of the words you don't like to use is the word "causation" or "causality," right?
>
> A Well, I use it rarely because it rarely applies. When it applies, I use it.
>
> Q Well, let's see if we can find someplace where we can agree. Does Celexa in high doses cause a prolongation of the QT interval?
>
> A In some patients yes, it would do that.
>
> Q Does Lexapro cause a reduction of the symptoms of depression or anxiety in some patients?
>
> A Yes. In some patients I might use that word, although we don't generally use it with efficacy results.

Exhibit 49 at 86:3-86:24 (Deposition of Dr. Joseph Camardo).

The fact is that even though epidemiological support is not *necessary* , it is present in this case. These include results found in both peer-reviewed studies and Dr. Healy's report. Exhibit 13 at 26, 31; Exhibit 26; Exhibit 27; Exhibit 30; Exhibit 38*;* Exhibit 39.

---

[41] Dr. Camardo is a Forest Rule 30(b)(6) witness with respect to suicide and Celexa/Lexapro. His deposition was taken on September 2, 2011.

As a final aside, in their memorandum Forest takes the following statement from Dr. Healy about "science" and presents it to the Court out of context: **"Forget the science. Forget the controlled trials**..."*See* Defendant Memorandum of in Support of Defendant's Motion to Exclude Testimony of Plaintiffs' Expert David Healy, MD, at 43. The true context as Dr. Healy explains is: If you're going to understand the phrase, you have to have the full context. And the full context is this:

> "...that controlled trials are extraordinarily important, they can illustrate the bias that both doctors and patients bring to therapeutics, but that they can also -- insofar as they have been used to persuade doctors and patients to disbelieve the evidence of their own eyes as regards to adverse events, they can be counterproductive, that we are at a point -- when it comes to adverse events generally, given that adverse events are now probably one of the leading causes of death in the U.S., there comes a point where people -- doctors and patients need to learn to believe the evidence of their own eyes again if a thing is happening. For instance, weight gain on the antipsychotics, the evidence of a doctor's or patient's own eyes is quite compelling, but the controlled trial data, the way the companies carve it up, often leads doctors to believe that the weight gain isn't happening. This is a point where people do need to believe the evidence of their own eyes and be skeptical about what appears to be the evidence base, that is the data that comes from controlled trials."

Exhibit 50 at 282:20-283:20 (Deposition of David Healy, M.D.).[42]

V. DR. HEALY'S CLINICAL TRIAL ANALYSIS IS NOT CHERRY PICKED.

Forest goes to great lengths to convince the Court that Dr. Healy cherry picked data to fit his opinions and obscured the truth about SSRI clinical trial data. They do this by cherry picking the evidence *they* present to the Court. First, Forest spends less than one page attacking the odds ratios that Dr. Healy computed on Page 26 of his report that show statistically significant increased risks of both suicide acts and completions for persons on SSRIs, *including Celexa*. Exhibit 13 at 26.

Defendant's argument is that Dr. Healy's rates are different from those he published in his peer-reviewed literature. Exhibit 38 at 164. Forest is right to spend such little time on this fight. The reality is that both his report and his peer-reviewed article give statistically significant increases of suicide and suicide acts for those taking SSRIs rather than placebo, even though the confidence intervals differ. Exhibit 13at 26; Exhibit 38 at 164. Why are these results different if he used the same Table 1? Exhibit 13 at 26; Exhibit 38 at 164. Although Dr. Healy was unable to explain exactly how the statistical software he used to perform these calculations came up with different results, the more important point is that they were still statistically significant results. Exhibit 50 at 160:18-162:4 9. And this says nothing, of course, about the multitude of Dr. Healy's peer-reviewed publications that contain statistically significant results.

Defendant's second argument against Dr. Healy's clinical trial analysis is that Dr. Healy somehow created the data presented in Table 1 of his expert report. Exhibit 13 at 26. To the contrary, this table was taken directly from the Khan *et al* study, and as been published by Dr. Healy in several peer-reviewed articles. Exhibit 44 at 333; Exhibit 38 at 166. Dr. Healy chose to use the smaller subset (Section B) directly from Khan *et al.* to create the Table rather than the larger set (Section A). He did this not because it fit his purposes, but because he believed it was more reliable:

> Q Okay. So if I understand it correctly you disagree with Khan's methodology in using patient exposure year, but you used the fact that patient exposure year data wasn't available in section A to only use the data from -- the subset of data in section B for inclusion in your analysis. Is that correct?
>
> A No, you haven't quite understood the point I'm making, which is that it appears, from what he's laid out here, that the company has a better handle on what happened to the patients in section B. In a great number of these trials, companies lose track of patients afterwards and they may well have gone on to commit suicide. In this they

> appear to be saying that in section B of the table here they're more sure of what the data -- rates of suicide and suicidal acts look like.

Exhibit 50 at 139:21-140:11.

* * *

> Q From a methodological perspective, that's what you do when you arrive at these conclusions. You cherry pick data from discrete places to try and arrive at figures that support your conclusions. Right?
>
> A Absolutely not, no. That's completely incorrect. And let me give you further reasons why the data in part A of this table are probably less reliable than the data in part B. What you've got is a large number of patients that enter into clinical trials of a drug. And according to compassionate use protocols, companies may maintain these patients on the drug for months or years afterwards. It would be inappropriate to include these patients in the segment or to handle patients who end up on the drug on that basis in the same framework as patients who have been entered into a clinical trial and drop out because of an adverse event.

Id. at 143:13-144:9. Thus, Dr. Healy's examined the dataset that was more reliable to perform this particular calculation. He voiced a logical reason for doing so and explained the methodological purpose behind it. The real truth is that Forest disagrees with Dr. Healy's opinions, but knowing this is not grounds for exclusion, *their lawyers* resort to desperate efforts of cherry picking statements in their own rights to give the false impression that Dr. Healy's methodology is unsound. This is not the case.

VI. THE GHOST WRITING AND HEALTH VOLUNTEER STUDY CRITICISMS ARE MERITLESS.

Forest expends a considerable bit of energy criticizing Dr. Healy for articulating the problems surrounding the ghost writing practices of other SSRI manufacturers and citing the healthy volunteer data. However, their criticisms are simply wrong.

A. Forest Had a Ghostwriting Budget for Celexa/Lexapro. Forest's petulant criticisms of Dr. Healy fall into the same category as Queen Gertrude from *Hamlet*, who said, "The

lady doth protest to much, methinks." First, Dr. Healy, in his deposition, did in fact provide a specific instance in which Forest was involved in ghostwriting that came to light in securities litigation against the Defendant:

Q How do you define a ghost written article?

A A ghost written article is an article that's commonly written by a person who writes articles for an agency working to the pharmaceutical industry, where often the medical writer, who's prepared the early drafts of the article, will -- their name won't feature on the authorship line of the article and that the people who do feature on the authorship line of the article will typically be people who haven't had much to do with the actual writing of the article.

Q In relation to the Wagner article, what agency wrote the article?

A I can't remember which agency wrote the article.

Q And the basis for your statement that an agency wrote the Wagner article is what?

A I believe it comes up in the deposition of Dr. Wagner in the securities case.

Q And when was the last time you saw that deposition?

A The last time I saw that deposition was a number of years ago.

Q Well, the case settled in 2008 and you would have returned all of the materials then, correct?

A That's correct.

Q Okay. But as you sit here today, you have a distinct recollection from testimony you last saw four years ago that Dr. Wagner testified that one of her articles was written by an agency of some type?

A Yes, that's, broadly speaking, the recollection I have.

Exhibit 50 at 54:14-55:20. Clearly, Dr. Healy identified a specific article that was revealed to be ghostwritten by Forest in other litigation under sworn oath. The fact that he was unable to identify the specific article by name goes to weight, not admissibility.

Moreover, there is abundant documentary evidence that Forest, like other SSRI manufacturers and drug companies, has "manufactured" scientific literature in support of Celexa and Lexapro. As stated in his affidavit, Dr. Healy was provided and reviewed evidence released by the United States Senate that showed that Forest's 2004 marketing plan included $100,000 for "[b]ylined articles [that] will allow us to fold Lexapro messages into articles on depression, anxiety and comorbidity developed by (**or ghostwritten for**) thought leaders." Exhibit 37 at 2-3 (Emphasis added); Exhibit 51 at 24 (Ghostwriting). Dr. Healy goes on to state that "[t]his is exactly the type of ghostwriting that I referred to in my report and deposition with which Defendant's counsel took such great umbrage." Exhibit 37 at 2-3. The practice is so widespread that it has drawn recent exposure by The Washington Post. FN 13, *supra*. No matter what Forest's lawyers may argue, the simple facts are that Forest spends substantial money on ghostwriting beneficial articles for its products, to specifically include Lexapro.

B. There Is a Pattern in SSRI "Healthy Volunteer" Studies. Forest cannot have it both ways. It cannot jump on the SSRI marketing bandwagon, touting the similarities of its two SSRI medications to others in the class, and then seek to exclude Dr. Healy's testimony because he observes that, in all of the other SSRI drugs' clinical trials that he has examined over the course of many years, there is evidence from the healthy volunteer studies that supports the general causation opinion in this case. As Dr. Healy has stated in his report, he has analyzed multiple health volunteer studies, for multiple SSRI drugs, from multiple pharmaceutical companies, and has found evidence throughout that (1) SSRIs cause precursors to suicide such as akathisia/agitation, and (2) that drug companies manipulated the health volunteer studies in such a way that they downplay or diminish safety signals. Exhibit 13 at 20-23. His opinion is that this industry wide reality likely does not differ in the health volunteer studies done by Forest. *Id*. at 20. In addition, if the Court only read

Defendant's Motion to Exclude Dr. Healy, you would be left with the impression that Dr. Healy's health volunteer calculations and opinions were drawn up on a cocktail napkin. In fact, they have been published in peer-reviewed literature, and despite Defendant's attempts to mislead the Court, reviewed in the context of a randomized control design. Exhibit 43 at 23-24.

Regardless, Dr. Healy made clear during his deposition that the healthy volunteer studies are not necessary for him to reach the opinions that Celexa and Lexapro can cause suicide in some people:

> Q With regard to the methodology that you've used in this case, if you set aside data from healthy volunteer studies, is it your opinion that Celexa and Lexapro data that you have reviewed indicates that there's an increased risk of suicide with the use of these drugs?
>
> A Absolutely. I think the data is very clear-cut that these drugs can cause people to commit suicide and you can come -- it's the responsible and reasonable conclusion to come to based on the clinical trial data that we have for these two drugs. Quite aside from any healthy volunteer data for any other drugs is that these two drugs cause people to commit suicide.

Exhibit 50 357:17-358:5.

VII. *MILLER* WAS A TRAVESTY IN 2001 AND IS STILL ONE TODAY.

Forest's key case authority for excluding Dr. Healy's opinion testimony is the ruling by Judge Vratil in *Miller v. Pfizer, Inc.*, 196 F.Supp.2d 1062 (D. Kan. 2002), *aff'd.* 356 F.3d 1326 (10th Cir. 2004). It cites the case as if it were holy writ precedent. Far from it. As the Tenth Circuit itself made clear in *Hollander v. Sandoz Pharmaceuticals Corp.*, 289 F.3d 1193, 1204, 1206 (10th Cir. 2002), "*Daubert's* effort to safeguard the reliability of science in the courtroom may produce a counter-intuitive effect: different courts relying on the essentially the same science may reach different results." Therefore, precedentially speaking, *Miller* stands for nothing more than a judicial affirmation of the breadth and scope of the trial judge's *discretion*. Forest ignores the opinions of

the other federal court, in the Tenth Circuit, which had admitted Dr. Healy's testimony over similar challenges. *Tobin v. Smithkline Beecham*. 164 F.Supp.2d 1278 (D. Wy. 2001).

That being said, the *Miller* court did exclude Dr. Healy's testimony. Moreover, it did so based on a report from independent, court-appointed experts. What should we make of that? The answer to that question requires us to put *Miller* into context. The undersigned counsel also represented the family of 13 year old Matt Miller who, after being on Zoloft for 7 days, hanged himself in a closet. Exhibit 5 at 1. Because of our faith in the scientific integrity and legitimacy of Dr. Healy, we suggested, prior to the very first Rule 16 conference that the Court should appoint independent experts under Rule 706 to advise the Court regarding the *Daubert* propriety of both sides' experts. *Id.* We also urged the Court to permit open discourse between the independent experts and the retained experts for both sides. *Id*.

The Court declined to do so. However, many months later she decided to appoint independent experts to advise her regarding Pfizer's *Daubert* challenge to Dr. Healy. *Id.* at 2. Rather than allowing the experts to have free dialogue among themselves, or, indeed, even allowing the court's independent experts to formulate their own areas of the concern, the judge delineated the questions as to which it wanted advice (derived largely from Pfizer's briefing).

There were two independent experts. Only one, Dr. Davis, had psychopharmacology expertise. Amazingly, when he raised data-oriented questions at the *Daubert* evidentiary hearing, the judge would not allow Dr. Healy to answer them. *Id.* The Court based its ruling on its own construction of Rule 26, holding, in essence, that because he was not prescient enough at the time he wrote his Rule 26 report to anticipate the independent experts' questions, then he would not be allowed to answer them. Here is the seminal colloquy from the *Daubert* hearing:

> DR. DAVIS: I think it's pretty clear that Dr. Healy is a distinguished clinician and has many publications so that he would meet that type of criteria. . . . And it may be an evolving field and that, so there is a matter of judgment. . . . And what I anticipated when I came today that Dr. Healy might present his calculations or there might be a lot of discussions of the techniques of the calculations. . . .
>
> THE COURT: Maybe I can shed some light on this, especially in regard to your comment that you maybe expected to hear some more full explanation of where the 2.19 figure was derived. This is part of where the intersection of law and science is maybe not clear to somebody coming in from the outside. But under our federal rules which govern pretrial proceedings, each side obviously has a chance to call their own experts who will testify, and there's a time set as part of the discovery process where each expert is required to produce a written report that states all of the opinions that expert will offer at the trial, and also the basis for the opinions. That has to be done by a certain time prior to trial. . . . So that's why, that's what my ruling was earlier, and that's why you haven't heard the Power Point presentation that was alluded to earlier.

Exhibit 6 at 389-92.[43]

Reasonably read, *Miller* should be limited to the very specific facts before the court at that time. This is not just argument from an ardent advocate. It has support from an unexpected source. As the attached Affidavit, sets forth, as a result of overtures made by Dr. Davis to Dr. Healy, the undersigned counsel has communicated with Dr. Davis about a similar motion filed by another drug company in an SSRI/suicide case. Although Dr. Davis did not want to serve as a retained expert for either side, and really did not want to become inundated with volumes of information, he did express a desire to write a "friend of the court" letter to Judge Kern. Exhibit 12 at 1. In this letter, he expresses his own opinions regarding Dr. Healy and the limited scope of his "unscientific" recommendations in *Miller*. *Id.*

[43] The true irony about the fact that Dr. Davis's concerns focused on relative risk calculations is that the independent experts' reports had already soundly rejected Pfizer's "relative risks must be 2.0+" argument, and, in fact, Pfizer had withdrawn its Motion *in Limine* #8 on that point. *See* 195 F.Supp.2d at 1073.

Additionally, as the Court considers Forest's repeated reliance on *Miller*, it is also important to remember that *Miller* has been superseded by a regulatory "verdict" from the FDA. *Miller* involved a 13-year old boy who suicided after being on Zoloft for seven days. In 2004, when the FDA Advisory Committees were looking into the question of the association between SSRI drugs and pediatric suicidality, Dr. Healy filed a lengthy letter with the FDA. Exhibit 7. Pfizer filed a 40+ page, anti-Healy brief with them in response. Both submissions were directed at the general causation question of whether or not Zoloft causes some children to commit suicide. Pfizer touted its *Daubert* victory in *Miller*, cited the court experts' report there, and made all of the same arguments that it made to the *Miller* court. After considering both Pfizer's diatribe and Dr. Healy's submission, the FDA concluded that "causality has been established," it ordered **BLACK BOX** warnings, and, in May 2005, it issued an advisory in which it cautioned that one in 50 kids on these drugs become suicidal "DUE TO DRUG." Exhibit 9 at 1; Exhibit 10 at 1. The **BLACK BOX** warning can still be found to this day on all antidepressant package inserts including Celexa and Lexapro. Exhibit 28 at 2-3; Exhibit 52 at 1. In light of this current state of things, the exclusionary decision in *Miller*, which deprived a family of its day in court regarding the death of their only son, can only be seen as a complete travesty of justice.

Conclusion

Because Dr. Healy's expert opinions are both reliable and relevant within the meaning of *Daubert* and its progeny, because they are framed in the context of the generally accepted Bradford Hill criteria, and because they are supported by a body of credible scientific evidence, both from the public domain as well as from Forest's secret coffers, his testimony should be ruled admissible in this case. And, as a corollary, Forest's Motion to Exclude Testimony of Plaintiff's Expert, David Healy, M.D., should be denied.

Respectfully submitted,

PERDUE KIDD & VICKERY

/s/ Arnold Anderson (Andy) Vickery
Arnold Anderson (Andy) Vickery
Texas Bar No. 20571800
510 Bering Dr., Suite 550
Houston, TX 77057-1469
Telephone: 713-520-2500
Facsimile: 713-520-2525
Email: andy@justiceseekers.com
Counsel for Plaintiffs
[Admitted *Pro Hac Vice*]

Christopher L. Coffin, Esq.
PENDLEY, BAUDIN & COFFIN, L.L.P.
24110 Eden Street
P. O. Drawer 71
Plaquemine, LA 70764
Telephone: 225-687-6396
Facsimile: 225-687-6398
Counsel for Plaintiffs

Certificate of Service

I certify that on this 30th day of November, 2012, Plaintiffs' Memorandum in Opposition to Defendant's Motion to Exclude Testimony of Plaintiff's Expert, David Healy, M.D. has been electronically filed with the Clerk using the CM/ECF system, which will automatically send email notifications of such filing to the following attorneys of record:

Joseph P. Thomas, Esq.
John R. Ipsaro, Esq.
ULMER & BERNE LLP
600 Vine St., Suite 2800
Cincinnati, OH 45202-2409
Attorneys for Defendants

/s/ Arnold Anderson (Andy) Vickery
Arnold Anderson (Andy) Vickery